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| 09/720,531 | 12/19/2000 | John Craig Smith | PM 275901 | 2393 |

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FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

| EXAMINER | |
|---|---|
| SWITZER, JULIET CAROLINE | |
| ART UNIT | PAPER NUMBER |
| 1634 | |

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/720,531 | SMITH ET AL. | |
| | Examiner | Art Unit | |
| | Juliet C. Switzer | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *4-7,9 and 12-30* is/are pending in the application.

4a) Of the above claim(s) *4-7,9-11 and 26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-25* is/are rejected.

7)☒ Claim(s) *15,19 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/2000* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I, further electing the SNP at position 42723 of EMBL Accession number U95626 in the paper filed 6/12/03 is acknowledged. The traversal is on the ground(s) that groups I, II, and IV relate to the same inventive concept: detection of certain defined SNPS. This is not found persuasive because there is no special technical feature that joins these three groups, as discussed specifically in the requirement for lack of unity. The relationship between groups I and II is that group II is drawn to nucleic acids containing polymorphisms and group I is drawn to methods for detecting polymorphisms in nucleic acids. Claim 4 is broadly drawn so as to encompass any nucleic acid that comprises a human CCR2 gene comprising a T at position 2385 and/or an A at position 2649. Such a nucleic acid is provided in the prior art (see JP 09238688 A, see nucleotides 780 and 1044). Thus, such nucleic acids cannot be considered a special technical feature that joins groups I and II, since the nucleic acids of claim 4 do not provide a special technical feature over the prior art. Further, the products of group IV are not joined to the methods of group because under the PCT rules the first method of using and the first named product are joined, and in this case the pharmaceutical packs of group IV are not the first named product. Further, the products are pharmaceuticals that are not used in the methods of group I.

The requirement is still deemed proper and is therefore made FINAL.

The amendment canceling claims 1-3 and 8 and adding claims 12-30 has been entered. Claims 26-30 are withdrawn from prosecution as they recite a grouping of polymorphisms other than the elected group of polymorphisms, which in this case contains the single elected

polymorphism. As set forth in the restriction requirement, and under the guidance of MPEP 803.04 (quoted in the restriction requirement) if the elected group of polymorphisms becomes allowable then claims which recite groups comprising the elected group will be rejoined. Thus, claims 4-7, 9-11, and 26-30 are withdrawn from prosecution. Claims 12-25 are examined herein.

***Specification***

2. The disclosure is objected to because of the following informalities: The specification and claims repeatedly refer to EMBL accession numbers instead of reciting sequences or sequence identifiers. This recitation is similar to the recitation of a trademark, in that the EMBL accession number does not represent a fixed disclosure of a sequence, but instead refers to a record that is constantly able to be updated and modified. Applicant should amend the specification to include the sequences which are referred to by EMBL accession numbers (and comply with the remainder of the sequence rules) and file a 132 declaration with evidence showing and stating that the newly filed sequence is identical to the sequence that was in EMBL at the time the invention was filed.

***Claim Objections***

3. Claims 15, 19, and 21 objected to because of the following informalities: The trademark "Taqman" should be entirely capitalized. Appropriate correction is required.

***Claim Comment***

4. It is further noted that a number of the claims recite trademarks which refer to nucleic acid assays that are well known within the art. Many of these trademarks are acronyms whose full recitation better describe the nature of the assay, and the claims would be clarified by using the full term to describe the assay instead of the trademarked acronym.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 12, 13, 14, 15, 16, 17, 18, and 24 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "a CCR-2 mediated disease" in claims 12 and 24 appears to represent new matter. This rejection applies when the claim is interpreted to mean that CCR-2 mediated disease is a disease mediated by the receptor encoded by the CCR-2 gene. For claim 12, the applicant points to page 3, lines 5-15 for support. This section sets forth that one aspect of the present invention is a method of diagnosis of a single nucleotide polymorphism in CCR-2 in a human, including those that have CCR-2 *ligand* mediated diseases, but does not set forth a step which requires a human identified as having or at risk for having a CCR-2 mediated disease (referring to the receptor only, and not the ligand).

For claim 24, applicant points to the same section and also pages 11-12, lines 20-5. The passage bridging pages 11-12 does not discuss CCR-2 mediated diseases either.

The specification at page 1 discusses CCR-2 ligand mediated diseases (p. 1, line 6), but does not appear to specifically discuss diseases that are mediated by CCR-2 in particular. CCR-2 is a chemokine receptor, and the ligand MCP-1 acts through this receptor (p. 1 of spec, lines 8-9). The specification teaches a number of diseases in which MCP-1 has been implicated, but does not set forth or suggest that these are "CCR-2 mediated diseases." To state ligand has been implicated in the pathophysiology of disease does not provide support for the concept that the diseases are receptor mediated as there are other possible avenues of action by which a ligand may be implicated that do not necessary mean the disease is mediated by the receptor. Thus, no specific basis for this limitation was identified in the specification, nor did a review of the specification by the examiner find any basis for the limitation. Since no basis has been identified, the claims are rejected as incorporating new matter.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 12-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-23 are indefinite because the preamble of the claim recites a method for determining the presence or absence of a single nucleotide polymorphism, but the method steps of the claims do not clearly set forth that this recited goal is accomplished. For example, claim

12 recites a final process step requiring a step of testing the sample to determine the identity of the nucleotide. The claims do not clarify how the testing step which results in determining the identity of the nucleotide results in determining the presence or absence of a single nucleotide polymorphism. That is, it is unclear how one practicing the invention knows from the testing step whether one has in fact determined the presence or absence of a single nucleotide polymorphism.

Claims 12-25 are indefinite over the recitation of EMBL accession numbers (U95626 in particular, with regard to the elected invention) because it is not clear as to what is encompassed by this phrase. The sequences listed in the EMBL database are continuously able to be updated and modified. Therefore, there is no single, fixed definition for the sequences presented as EMBL Accession U95626, and thus the claim is indefinite for the recitation of the EMBL accession because the metes and bounds of the claim cannot be determined.

Claims 22, 23, 24, and 25 are also indefinite because it is unclear what is meant by a position "corresponding" to position 42723 of EMBL ACCESSION NO. U95626. That is, is applicant referring to position 42723 of EMBL ACCESSION NO. U95626 or are other positions within EMBL ACCESSION NO. U95626 within the scope of this recitation? To have a position "corresponding" to position 42723 of EMBL ACCESSION NO. U95626, does a nucleic acid simply have to have 42723 nucleotides or is some other structural limitation implied by the use of this language?

***Enablement Rejection 112, 1st paragraph***

9. Claims 12-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

**Nature of the Invention and Breadth of the Claims**

Claims 12-23 are drawn to methods for determining the presence or absence of a polymorphism at position 42723 of EMBL ACCESSION NO. U95626. Claims 24-25 recite methods of characterizing the genotype of a human and include a step of determining the identity of a nucleotide at position 42723 of EMBL ACCESSION NO. U95626. The specification teaches that 42723 of EMBL ACCESSION NO. U95626 is within the promoter of the human CCR-2 gene (p. 3, lines 9-12). The polymorphism being detected is an C→A transition within the promoter of the human CCR-2 gene.

Furthermore, rejected claims 12-18 and 24 require that the nucleic acid sample assayed be obtained from an individual identified as having or at risk of having a "CCR-2 mediated disease." Thus, the nature of the claimed invention requires knowledge of the identity of diseases which are in fact mediated by P2X7.

**State of the Art**

The prior art teaches the nucleic acid sequence of the genomic and cDNA of the human CCR-2, and that this receptor is chemokine receptor (see Smith *et al.* (1997) and Wong *et al.* (1997), for example).

The prior art does not establish any relationship between the polymorphism at position 42723 of EMBL ACCESSION NO. U95626 and any particular disease, disease state, phenotype, or activity. The prior art further does not demonstrate any relationship between any polymorphism within the promoter of the human CCR-2 gene and any phenotype.

Furthermore, with regard to the concept of "CCR-2 mediated disease," the prior art teaches that HIV-1 infected individuals carrying a CCR2-64I allele progressed to AIDS 2 to 4 years later than individuals without the allele, though the prior art does not specifically teach that this gene "mediates" the disease (Smith *et al.*, 1997).

**Direction Provided and Working Examples**

The specification teaches a single nucleotide polymorphism that is an C→A transition within the human CCR-2 promoter at a position that corresponds to 42723 of EMBL ACCESSION NO. U95626. The specification teaches that within a sample of 20 individuals the C allele is present 70% of the time (p. 19). The specification demonstrates detection of this polymorphism via direct sequencing of PCR products and also teaches that the polymorphisms can be detected via engineering of position 42724 (A-G) to create a Mae II recognition site (p. 24). Beyond this, the specification provides no further specific guidance with regard to this elected polymorphism.

Based on the teachings of the specification, one would not know how to use the claimed invention because one does not know the relevance of detecting the recited mutation.

The amount of direction or guidance presented in the specification with regard to how to use the instant invention is minimal. That is, the specification does not provide any guidance as to how the polymorphism at position 42723 of EMBL ACCESSION NO. U95626 would be associated with any pharmaceutical agent. The specification does not discuss whether this particular polymorphism will increase the likelihood of a positive or negative response to any drug. The specification provides no guidance or working examples that teach or demonstrate the

ability to use the disclosed polymorphic site as a marker for any disease in particular, or for disease in general, or how to use the disclosed polymorphism to select a proper course of treatment of a disease.

The specification asserts that the ligand for the receptor CCR-2 has been "implicated" in a number of diseases, including those listed in claim 14, for example (p. 1). The specification does not discuss diseases that are mediated by the receptor itself, as opposed to by the ligand, or how to identify a risk of having such diseases. The specification does not provide any working examples of methods for identifying patients as having or at risk of having CCR-2 mediated diseases. Furthermore, the specification does not disclose any relationship between CCR-2 mediated diseases and the polymorphism at position 42723 of EMBL ACCESSION NO. U95626. While the specification does refer generically to "CCR-2 ligand mediated" diseases, the specification does not particularly define what is required for a disease to be mediated by a CCR-2 ligand let alone to be mediated by the receptor CCR-2.

**Level of Skill in the art, Level of Unpredictability, and Quantity of Experimentation**

The level of skill in the art is quite high, but the unpredictability in the art is higher. There is no way of predicting which diseases, of the variety of possibilities proposed in the specification, are in fact "CCR-2 mediated." This is especially pertinent when considering that the polymorphism was observed 30% of the time in a sample of 20 individuals who are not identified as having any particular diseases.

There is also a large body of knowledge in the prior art related to polymorphisms in general, and their association with diseases or disease states. The art is highly unpredictable with regard to the functionality of polymorphic sites in genomic DNA. After a screening assay

identifies polymorphisms, it is unpredictable whether any such polymorphisms would be associated with any phenotypic trait, such as a disease state or a physiological state. For example, Hacker et al. were unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (Gut, 1997, Vol. 40, pages 623-627). Even in cases where an association between a particular gene and a disease state is known to exist, such as with the LPL gene and heart disease risk or the β-globin gene and sickle cell anemia, researchers have found that when using SNP (single nucleotide polymorphism analysis) it was difficult to associate SNPs with disease states or to even identify key genes as being associated with disease (Pennisi, Science, 281 (5384):1787-1789). Finally, in some cases where multiple polymorphisms are identified in a gene, some of these are demonstrated to be disease associated and some are not. Blumenfeld et al. (WO 99/52942) disclose a number of polymorphisms in the FLAP gene. While Blumenfeld et al. were able to demonstrate that some of these polymorphisms are associated with patients having asthma but some of these are not (see Figure 3). For example, the marker 10-35/390 was demonstrated to be associated with asthma, with a p value of 0.00229, while the marker 10-33/327 was determined to not have a statistical association with asthma (p=0.294). Thus, even for SNPs within the same gene, it is highly unpredictable as to whether a particular marker will be disease associated.

The significance of the instantly disclosed CCR-2 polymorphism remains highly unpredictable, as neither the specification nor the prior art demonstrate that this polymorphism is related to any disease or has and effect on CCR-2 gene function. Thus determining how to use the claimed methods as asserted by applicant, requires the knowledge of unpredictable and

potentially non-existent associations between the polymorphism and some disease or disease state. Even if the elected polymorphism is in some way associated with some disease, it is difficult (if not impossible) to know or predict from the teachings of the specification which disease or how the polymorphism is associated. That is, it is unpredictable as to whether the presence of a particular allele the polymorphism would confer a higher or lower likelihood of having the disease. In this case, the possible uses for the claimed methods are undefined, beyond the suggestion that they can be used to detect a disease associated with the CCR-2 gene prior to treatment with a CCR-2 ligand drug.

The quantity of experimentation required to discover how to use the instant invention is very high. In order to use the claimed invention as asserted by the specification, one would have to establish a relationship between the polymorphism at position 42723 of EMBL ACCESSION NO. U95626 and some disease state or some disease treatment method. Indeed, even to use the method of claim 12 to identify patients suited for particular pharmaceutical agents, one would need to know that the polymorphism at nucleotide 42723 of EMBL ACCESSION NO. U95626 was in some way associated with response to some pharmaceutical agent. In order to obtain the type of information necessary to practice the claimed invention, one would be required to undertake the screening of hundreds or thousands of patients as well as possible hundreds of diseases or pharmaceutical agents. Even if such experiments were undertaken, it would still be unpredictable as to whether any associations would be detected, in light of the unpredictability of such associations, as already discussed. Thus, while one could perform further research to determine whether applicant's method would be useful in disease detection and/or treatment, it is unknown as to what the outcome of such research might be and as to whether any quantity of

experimentation would result in the identification of an association between the CCR-2 42723 polymorphism and any disease or condition. Likewise, with respect to the claims that recite "CCR-2 mediated disease" in general or a list of diseases in particular, it is be unpredictable as to whether the instant polymorphism is in fact linked to any disease state or treatment response. Further, absent a teaching the polymorphism at position 42723 of EMBL ACCESSION NO. U95626 is not associated with such conditions, it is further unpredictable as to whether detection of the polymorphism would be useful in predicting, e.g., the absence or decreased likelihood of such conditions.

Furthermore, there is no way of predicting which diseases, of the variety of possibilities proposed in the specification, are in fact "CCR-2 mediated." Absent any specific guidance from the specification or the prior art, in order to practice the claimed invention, one would have to undertake extensive studies to confirm the fact that the any particular disease, let alone all of the diseases recited in claim 14, is in fact a "CCR-2 mediated disease." One would have to undertake extensive biochemical analysis of patients who have the diseases in order to determine the etiology of the disease and the role of the receptor CCR-2.

**Conclusion**

Thus, in light of the nature of the invention, the state of the art, the high level of unpredictability in the art, the lack of direction or working examples in the specification, and the high quantity of experimentation that would be required to practice the claimed invention, it is concluded that undue experimentation would be required to use the instantly claimed invention. Thus, after careful consideration of all of these factors, it is concluded that the practice of the

claimed invention would require undue experimentation in order to determine how to make and use the claimed invention.

***Claim Rejections - 35 USC § 101/112 1st paragraph***

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 12-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 12-23 are drawn to methods for determining the presence or absence of a polymorphism at position 42723 of EMBL ACCESSION NO. U95626. Claims 24-25 recite methods of characterizing the genotype of a human and include a step of determining the identity of a nucleotide at position 42723 of EMBL ACCESSION NO. U95626. The specification teaches that 42723 of EMBL ACCESSION NO. U95626 is within the promoter of the human CCR-2 gene (p. 3, lines 9-12). The polymorphism being detected is an C→A transition within the promoter of the human CCR-2 gene. There is no well established utility for the claimed invention.

The specification asserts that the "One approach is to use knowledge of polymorphisms to help identify patients most suited to therapy with particular pharmaceutical agents (p. 2)," but the specification does not provide any evidence that the polymorphism at position 42723 of EMBL ACCESSION NO. U95626 is in fact correlated with patient response to any particular pharmaceutical agent. The specification further asserts that "individual who carry particular allelic variants of the CCR-2 gene may therefore exhibity differences in their ability to regulate

protein biosynthesis under different physiological conditions (p. 8)," however no showing is provided that this phenomena occurs with respect to the polymorphism at position 42723 of EMBL ACCESSION NO. U95626 in particular. The specification asserts at page 8 that humans may be tested for predisposition or susceptibility for disease (lines 27-28), but the specification does not provide any evidence that the polymorphism is associated with any particular human disease. The specification asserts that the claimed methods can be used in the development of new drug therapies stating that "Identification of a link between a particular allelic variant and predisposition to disease development or response to drug therapy may have a significant impact on the design of new drugs (p. 29)" but again, the specification fails to provide of a link between a particular allelic variant and predisposition to disease development or response to drug therapy. The specification asserts that the polymorphisms can be used in genetic markers in linkage studies (p. 14). None of these asserted utilities are specific to the methods claimed herein, because any method of detecting a polymorphism in a gene can be used to determine if any of these relationships exist between the polymorphism and putative related diseases. Any polymorphism can generically be asserted as being useful in a linkage study. None of these asserted utilities are substantial in view of the claimed methods because they all require further experimentation to reasonably confirm that such a utility exists. The asserted utilities for methods of the claimed invention are an invitation to the practitioner to determine if in fact a specific and substantial utility exists for the disclosed invention.

Claims 12-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a

well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Claim Rejections - 35 USC § 103***

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 12, 13, 14, 24, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong *et al.* in view of Sozzani *et al.*

This rejection applies to these claims insofar as HIV-1 infection is considered a "CCR-2 mediated disease."

With regard to claim 12, Wong *et al.* teach a method which comprises the steps of:

(a) providing a nucleic acid sample from a human wherein the sample comprises a nucleotide at position 42723 of EMBL ACCESSION NO. U95626; and

(b) testing the sample to determine the identity of the nucleotide.

With regard to claim 13, the nucleic acid sample comprises a fragment of a CCR-2 DNA.

With regard to claims 24 and 25, Wong *et al.* teach a method which comprises the steps of:

(a) providing a nucleic acid sample from a human wherein the sample comprises a nucleotide at position 42723 of EMBL ACCESSION NO. U95626;

(b) testing the sample to determine the identity of the nucleotide; and

(c) recording the identity of the nucleotide in a print- or machine readable medium.

In particular, Wong *et al.* sequence the gene encoding human CCR-2, including a portion of the 5' untranslated region and teach that the nucleotide sequences of these regions were given in GenBank Accession number U80923 and U80924 (p. 1039). The sequenced region of the 5' untranslated portion includes the region of the CCR-2 promoter that includes position 42723 of EMBL ACCESSION NO. U95626 (As evidence of this the GenBank record is included with this office action. At least nucleotides 62-102 of the Wong *et al.* sequence are identical to nucleotides 42703-42743 of EMBL ACCESSION NO. U95626, thus including a portion that overlaps with position 42723). Sequencing of the CCR-2 gene inherently determines the identity of the nucleotide at each position sequenced. Recording the sequence as a GenBank record meets the limitation of step (c) of claims 24 and 25, since the GenBank is available as a computer readable medium.

Wong *et al.* do not teach a method wherein the sequenced nucleic acid is obtained from a human having or at risk of having a CCR-2 mediated disease (generically) or any of the specific diseases as listed in claims 14 or 25.

Smith *et al.* teach methods wherein teh CCR-2 gene is screened for mutations in order to further elucidate the function and relationship of the receptor CCR-2 to HIV-1 infection. Smith *et al.* utilize a single stranded conformation polymophism/heteroduplex assay to screen the entire CCR-2 gene.

It would have been prima facie obvious to one of ordinary skill in the art to have modified the methods taught by Wong *et al.* so as to have included DNA samples from patients having or suspected of having HIV-1 infection, so as to have further elucidated the function and relationship of the receptor CCR-2 to HIV-1 infection. One would have been motivated to sequence the CCR-2 gene of HIV infected individuals in order to have applied the sequencing method taught by Wong *et al.* to the search for polymorphisms in the CCR-2 gene as taught by Smith *et al.*, thus providing an additional use for the sequencing methods taught by Wong *et al.*

***Conclusion***

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C Switzer
Examiner
Art Unit 1634

September 28, 2003